

Early-Life Environmental Risk Factors for Asthma: Findings from the Children's Health Study

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Early-life experiences and environmental exposures have been associated with childhood asthma. To investigate further whether the timing of such experiences and exposures is associated with the occurrence of asthma by 5 years of age, we conducted a prevalence case-control study nested within the Children's Health Study, a population-based study of > 4,000 school-aged children in 12 southern California communities. Cases were defined as physician-diagnosed asthma by age 5, and controls were asthma-free at study entry, frequency-matched on age, sex, and community of residence and counter-matched on *in utero* exposure to maternal smoking. Telephone interviews were conducted with mothers to collect additional exposure and asthma histories. Conditional logistic regression models were fitted to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Asthma diagnosis before 5 years of age was associated with exposures in the first year of life to wood or oil smoke, soot, or exhaust (OR = 1.74; 95% CI, 1.02–2.96), cockroaches (OR = 2.03; 95% CI, 1.03–4.02), herbicides (OR = 4.58; 95% CI, 1.36–15.43), pesticides (OR = 2.39; 95% CI, 1.17–4.89), and farm crops, farm dust, or farm animals (OR = 1.88; 95% CI, 1.07–3.28). The ORs for herbicide, pesticide, farm animal, and crops were largest among children with early-onset persistent asthma. The risk of asthma decreased with an increasing number of siblings ($p_{\text{trend}} = 0.01$). Day care attendance within the first 4 months of life was positively associated with early-onset transient wheezing (OR = 2.42; 95% CI, 1.28–4.59). In conclusion, environmental exposures during the first year of life are associated with childhood asthma risk. **Key words:** asthma, breast-feeding, cockroach, day care, farm environment, herbicide, pesticide, sibship size, wood smoke. *Environ Health Perspect* 112:760–765 (2004). doi:10.1289/ehp.6662 available via <http://dx.doi.org/> [Online 9 December 2003]

Asthma is the most common chronic disease among U.S. children (Mannino et al. 1998) and is the leading cause of childhood morbidity as measured by hospitalizations and school absences (Weiss and Sullivan 2001). Although a large number of studies of asthma have been conducted, the etiology of childhood asthma remains to be firmly established.

An accumulating body of evidence indicates that both lifestyle factors and environmental exposures during early life may play particularly important roles in asthma occurrence (Johnson et al. 2002). Moreover, timing of such environmental exposures during early development may also be critically important in allergic sensitization and later asthma development. For example, the risks for asthma development associated with exposure to pets, cockroaches, or farming environment appear to vary by age at exposure. Children exposed to cats in the first 2 years of life were sensitized to cat by age 4 and were at increased risk of severe asthma in the presence of secondhand tobacco smoke (Melen et al. 2001). Cockroach sensitization, which often occurs at a very early age in exposed children (Alp et al. 2001), has been associated with increased risk of incident asthma (Litonjua et al. 2001). In a farming environment, children exposed to stables in the first year of life had reduced risk of asthma compared with children who had such exposure after 1 year of age (Riedler et al. 2001). Although early exposure to endotoxin from farm environment is associated with reduced

childhood asthma risk (Braun-Fahrlander 2001), endotoxin exposures later in life may increase asthma occurrence, especially in agricultural settings (Schwartz 2001).

Given the emerging evidence for age-dependent effects of early-life environmental exposures and lifestyle factors in childhood asthma etiology, we hypothesized that environmental exposures in early childhood, especially during the first year of life, are associated with increased occurrence of early transient wheezing and/or early persistent asthma. We further hypothesized that early-life experiences including infant feeding practices, greater sibship size, and day care attendance influence the risk of early childhood asthma. To assess these hypotheses, we conducted a case-control study of risk factors for early-life asthma that was nested in the Children's Health Study (CHS), a population-based study of children's respiratory health in 12 southern California communities.

Materials and Methods

Subject selection. Subjects for this case-control study were selected from the CHS. Details of the CHS have been described previously (Peters et al. 1999a, 1999b). In brief, the CHS is a population-based study in which 6,259 children were recruited from public school classrooms from grades 4, 7, and 10 in 12 communities in southern California. The average classroom participation rate was 82%. The parents or guardians

of each participating student provided written informed consent and completed a self-administered questionnaire.

We used a counter-matched sampling design (Langholz and Goldstein 2001) to select subjects for this nested case-control study. Our study base consisted of 4,244 of the 6,259 children, who were between 8 and 18 years of age at the time of enrollment in the CHS and had completed active follow-up at schools. From these 4,244 children, we selected all children with asthma who had been diagnosed with asthma before 5 years of age ($n = 338$). Matched controls were asthma-free children and were selected randomly from each of the 96 grade-, sex-, and community-specific strata based on the number of cases in each stratum and the cases' *in utero* exposure to maternal smoking status. The number of asthma-free controls ($n = 570$) provided approximately equal numbers of children who were exposed or unexposed to maternal smoking within each sampling stratum. During the study period, mothers of 82.5% cases ($n = 279$) and 72.3% controls ($n = 412$) participated; the remaining mothers could not be located or were unwilling to be interviewed. This resulted in a sample of 691 subjects, with 279 cases and 412 controls. The University of Southern California Institutional Review Board reviewed and approved the study. All subjects gave informed consent.

Data collection. The biologic mother of each case and control provided detailed information on demographics, family history of asthma, feeding practices in infancy, day care attendance, household environment (pets, cockroaches, and wood smoke, oil, or exhaust), and farm related exposures (crops or dusts, farm animals, herbicide, and pesticides) by a structured telephone interview. In the absence of biologic mother (i.e., 4.7% of the cases and 9.7% of the

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